ABSTRACT

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Title of Diploma Thesis: Identification of new potent inhibitors of selected mycobacterial enzyme

Mycobacterium tuberculosis remains one of the deadly pathogens, which are threat for people around the world. The combination of antituberculotic drugs is effective but the treatment is prolonged and sometimes it is not successful because of multiresistant forms of tuberculosis and also co-infection with HIV, that are the problems in last a few years. Therefore, it is necessity to find a new drug against tuberculosis, which will be effective against resistant forms of mycobacterium and can be used for HIV therapy. Enzyme isocitratelyase performs a potentially drug target against *Mycobacterium tuberculosis*. This enzyme plays a key role of glyoxylate pathway, where catalyzes the conversion of isocitrate to succinate and glyoxylate. This enzyme is necessary for mycobacterial survive during acute phase of the infection.

The aim of this work is to determine that the activity of isocitratelyase is inhibited by *S*-benzylisothiosemicarbazones and flavonoids and so they could be new potentially antituberculotic drugs.

Activity of this enzyme was determined by spectrofotometric method in our research and discovered on the basis of glyoxylate´s quantity in well plates.

Results of our study have shown low inhibition property of flavonoids - the most inhibit isocitratelyase (-)-epigallocatechine gallate and quercetin hydrate. These compounds of the group of *S*-benzylisothiosemicarbazones have had the most ability to inhibit isocitratelyase: 5-bromosalicylaldehyde-*S*-4-fluorbenzylisothiosemicarbazone, benzaldehyde-*S*-4-brombenzylisothiosemicarbazone, salicylaldehyde-*S*-4-chlorbenzylisothiosemicarbazone and salicylaldehyde-*S*-4-bromobenzylisothiosemicarbazone.